PROJECT REPORT
COMMITTEE ON FOOD RESEARCH

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"Effect of Stress Factors on Nutrition"

SUMMARY

Objectives

Available evidence indicates that in addition to the major nutrients, substances are present in our diet which may be required in increased amounts during conditions of stress. Such factors are apparently dispensable under normal conditions or their requirements are so small they may be readily met by amounts present in the diet or through the synthetic activity of the intestinal flora or the animals' own tissues. Certain drugs or other "stress factors" may, however, increase requirements for these substances to the extent that deficiencies occur, manifest by retarded growth or tissue pathology, and preventable by the administration in appropriate amounts of the missing nutrient. The purpose of experiments undertaken under the present contract was to continue studies previously initiated on the effects of various "stress factors" on the nutritional requirements of the rat.

Scope of the assigned project

Stress factors studied in the present investigation include the following:

(1) Accelerated metabolism resulting from thyroid feeding
(2) Accelerated metabolism resulting from exposure to low environmental temperature
(3) Administration of toxic doses of atabrine (quinacrine HCl)
(4) Administration of excessive doses of thiamine, riboflavin and nicotinic acid under conditions of ad libitum and reduced caloric intake.

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Major results obtained

(1) Toxic doses of thyroid increased requirements for at least one unknown nutrient in the immature female rat. Desiccated whole liver counteracted completely the retardation of growth and inhibition of ovarian development observed in immature female rats fed toxic doses of thyroid. It also prolonged significantly the average length of survival of the immature thyroid-fed rat. Brewers' type yeast and cholesterol were also effective in prolonging survival of immature thyroid-fed rats; these substances were ineffective, however, in counteracting retardation of growth or inhibition of gonadal development. The protective factor in whole liver was present in the water-insoluble fat-free residue of desiccated whole liver. It is heat stabile and distinct from any of the known nutrients.

(2) Continuous exposure to low environmental temperatures increased requirements for at least one unknown nutrient in the immature rat. Immature female rats were raised to maturity under cold room and room temperature conditions on purified rations containing the B vitamins as synthetic factors and as present in whole liver and yeast. Growth was markedly reduced in all rats under cold room conditions; animals fed desiccated whole liver, however, gained significantly more weight than these fed other diets employed. The protective factor(s) was distinct from any of the known B vitamins and was not present in significant amounts in yeast. At room temperature conditions no significant difference in growth occurred on any of the diets tested.

(3) Toxic doses of atabrine increased requirements for at least one unknown nutrient in the immature rat. Immature female rats were maintained for 8 weeks on purified rations containing 500 mg of atabrine per kg of diet, and the effects of feeding were contrasted with that observed on similar rations with atabrine omitted. Four experimental rations were employed: (1) a basal ration containing the B complex factors in synthetic form only (2) the basal ration plus additional B vitamins (3) the basal ration plus yeast and (4) the basal ration plus desiccated whole liver. The effects of atabrine feeding differed significantly on the various diets employed. Administration of atabrine plus basal ration resulted in a marked retardation of growth, alopecia, inhibition of ovarian develop-

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ment, enlarged submaxillary glands, granulocytosis and myocardial damage as indicated by electrocardiographic tracings. These effects were largely counteracted by diets containing whole liver and yeast and to a lesser extent by the administration of additional B vitamins. On atabrine-free rations no abnormalities were observed on any of the diets employed. Desiccated whole liver was more effective than yeast or the additional B vitamins in promoting growth and ovarian development in the immature atabrine-fed rat. The protective factor(s) was present in the water-insoluble fraction of liver remaining after removal of the extractable water-soluble material.

(4) No adverse effects of vitamin imbalance as caused by massive doses of thiamine, riboflavin and nicotinic acid were observed in female rats over a 20 week period under conditions of ad libitum feeding or at a caloric restriction of 50 %. Measurements were made of R.B.C., Hb., total W.B.C. and differential counts, body weight changes, basal metabolic rate and gross appearance.

Implications of the work

These findings indicate that many diets which are apparently adequate under "normal" conditions become inadequate under certain conditions of stress. Where metabolism is increased after excessive thyroid feeding or prolonged exposure to cold, or after administration of massive doses of atabrine, toxic effects occur on apparently adequate diets. These effects may be largely, if not completely, counteracted by dietary means, more specifically by an apparently unknown factor or factors present in whole liver. Members of the armed forces are on occasion exposed to conditions of stress similar to those employed in the present experiments. Information as to how these "stress factors" may affect nutritional requirements would be of distinct value in the feeding of exposed personnel.

Plans for further investigation

Further investigations are planned along the following lines: (1) concentration, isolation and identification of the protective factor or factors in desiccated whole liver effective in counteracting the above effects and (2) effects of other stress factors such as chlorinated water, various drugs, etc., on the nutritional requirements of the rat.

Publications resulting from above investigations.

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(5) Smith, E.D., Ershoff, B.H., Winzler, R.J., and Deuel, H. J. Jr., Effects of B vitamins, liver and yeast on growth under cold room and room temperature conditions. J. Nutrition, January, (1948)

(6) Ershoff, B.H., The effects of B vitamins, liver and yeast on atabrine toxicity in the rat. J. Nutrition, February (1948)

(7) Ershoff, B.H., and Walter Marx Effects of cholesterol feeding on the length of survival of immature rats fed toxic doses of thyroid. In press.